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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,378	10/05/2006	Masayo Takahashi	12480-000147/US	3138

30593 7590 03/08/2007

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EXAMINER	
MACFARLANE, STACEY NEE	
ART UNIT	PAPER NUMBER
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,378	TAKAHASHI ET AL.	
	Examiner	Art Unit	
	Stacey MacFarlane	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/29/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Application is a national stage entry of PCT/JP04/03848, filed March 22, 2004, further claiming foreign priority to Japanese application 2003-096002, filed March 31, 2003, a certified copy of which has been filed.

Claim Objections

2. Claim 1 is objected to because of the following informalities: the Claim uses the acronym "ES" without first identifying the cells by the complete name. Appropriate correction is required.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 8, 16 and 19 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Without evidence to the contrary, the lens cells produced by the claimed method read upon lens cells that are substantially identical to those found in humans and thus reads upon cells in a human being. Indeed, the disclosure recites that the method claimed produces "lens cells that are closer to the natural lens cells" than those produced via immortalization processes (page 2, last paragraph, last line). Further, the specification also discloses that transplant of such cells into people (pages 1-2). The claims, therefore, also read on human beings having such cells transplanted into them. Thus, the claimed invention reads upon unpatentable

subject matter. Amending the claim to include evidence of the hand of man (i.e. by specifically reciting that the lens cell is "isolated") would be remedial.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-4, 6-9, 11, and 14-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawasaki et al. *Generation of dopaminergic neurons and pigmented epithelial from primate ES cells by stromal cell-derived inducing activity*, Proceedings of the National Academy of Sciences USA 99(3):1580-1585, published on February 5, 2002, which is more than one year prior to the earliest US filing date of instant application.

5. The reference teaches methods of culturing and differentiating pluripotent cynomolgus monkey embryonic stem (ES) cells and recites the exact steps claimed as the method of the instant application. In the Materials and Methods section (bridging pages 1580-1581), the reference teaches both a "maintenance" step and a "differentiation" step. The maintenance step of the prior art teaches undifferentiated primate ES cells, derived from the cynomolgus monkey, were maintained with a medium containing "4ng/ml basic fibroblast growth factor". This fully anticipates the limitations of Claims 1, wherein it states "an ES cell maintenance step of maintaining an ES cell by using a medium containing a fibroblast growth factor FGF-2 at a

concentration of 2ng/ml to 50 ng/ml", and the limitation of Claim 4 where it recites the method of claim 1 "wherein in the ES cell maintenance step, the medium contains the fibroblast growth factor FGF-2 at a concentration of 4ng/ml to 50 ng/ml." It is common knowledge in the art that FGF-2 of the claim is equivalent to the "basic fibroblast growth factor" of the reference. Fibroblast growth factor was first identified from cow pituitary extract by Gospodarowicz et al. in 1974, who further fractionated the extract using acidic and basic pH (*Proceedings of the National Academy of Sciences USA* 71(6):2295-2299, 1974), thus isolating two slightly different forms termed "acidic fibroblast growth factor" and "basic fibroblast growth factor", and since regarded in the literature as FGF-1 and FGF-2, respectively.

6. Further, Claim 1 recites a "differentiation step" carried out after the maintenance step which comprises of "inducing differentiation of the ES cell into a lens cell by implanting and culturing the ES cell on a mouse skull cell [line] PA6 at a density of 2 colonies/cm^2 to 6.5 colonies/cm^2". The disclosure of the application recites a "cell density of 2 to 6.5 (colonies/cm^2) is equivalent to about 150 to 500 colonies when converted into the number of colonies per culture dish, 10 cm in diameter" (page 9, lines 1-4). The prior art teaches an identical differentiation step that comprises of ES cells "plated on PA6 cells at a density of 500 clumps/10 cm dish" (page 1581, column 1, lines 8-10). It would be immediately apparent to one of ordinary skill in the art of cell culture that the "colonies" of the claim are equivalent to the "clumps" of cells described by the reference. Thus, the prior art fully anticipates the limitations of Claim 1.

7. Claim 2 of the instant application recites the method of Claim 1 "further comprising a washing step, carried out between the ES cell maintenance step and the differentiation inducing step, of washing the maintained ES cell once with an ES differentiation medium". The claim of the application uses the term "comprising of", which is an open term interpreted as not excluding additional, un-recited elements or method steps (see MPEP section 2111.03). Thus, the prior art anticipates the limitation of Claim 2 wherein it teaches a step carried out between maintenance and differentiation steps in which the "undifferentiated ES cell colonies were first washed twice with ....differentiation medium" (page 1581, column 1, lines 2-6).

8. Claim 3 of the instant application recites the method of claim 2 "wherein the differentiation inducing medium used for inducing differentiation of the ES cell into a lens cell is used as the ES differentiation medium". This is fully anticipated by the prior art wherein it teaches that the medium defined as "differentiation medium" (page 1581, column 1, lines 3-6) is the same medium in which the ES cells are cultured during the differentiation inducing step of the method (page 1581, column 1, lines 8-10).

9. Claim 6 recites the method of Claim 1 "wherein the ES cell is derived from primates" and Claim 7 recites the method of Claim 6 "wherein the ES cells is derived from cynomolgus monkey". As stated above, the prior art teaches (line 1 of the Materials and Methods section of page 1580) anticipates the method of Claim 1 and teaches said method using "primate ES cells", and specifically, "cynomolgus monkey ES cell[s]".

10. Claim 9 recites the method of Claim 2 wherein the medium used during maintenance step "contains the fibroblast growth factor FGF-2 at a concentration of 4ng/ml to 50ng/ml". This is anticipated by the prior art that teaches the method of Claim 2 carried out with medium containing "4ng/ml basic fibroblast growth factor" (page 1580, section entitled "Maintenance of Primate ES Cells", lines 8-9). Claim 11 recites the method of Claim 3 wherein, in the ES cell maintenance step, the medium "contains the fibroblast growth factor FGF-2 at a concentration of 4ng/ml to 50ng/ml". This is anticipated by the prior art, which teaches the method of Claim 3 performed with medium containing "4ng/ml basic fibroblast growth factor" during the maintenance step(supra).

11. Claim 14 recites the method of Claim 2 "wherein the ES cell is derived from primates" and Claim 15 recites the method of Claim 14 "wherein the ES cell is derived from cynomolgus monkey". The prior art anticipates the method of Claim 2 and teaches this method carried out in "primate ES cells", and specifically, "cynomolgus monkey ES cell[s]" (line 1 of the Materials and Methods section of page 1580).

12. Claim 17 recites the method of Claim 3 "wherein the ES cell is derived from primates, and Claim 17 recites the method of Claim 17 "wherein the ES cell is derived from cynomolgus monkey". The prior art anticipates the method of Claim 3 and teaches that it is carried out in "primate ES cells", specifically, "cynomolgus monkey ES cell[s]" (line 1 of the Materials and Methods section of page 1580).

13. Claims 8, 16 and 19 are drawn to the lens cell produced by the methods claimed. Since the claim language is drawn to the cell produced by the method and does not

specify distinguishing features or characteristics of said cell, it is anticipated by the Kawasaki reference. The reference fully anticipates each step of the methods claimed, and teaches that the cells produced by this method can also give rise to dopaminergic neurons and pigmented epithelial cells. Lens cells are among the cells that are produced by the claimed method. The reference, therefore, inherently teaches the claimed product. Section 2112.01 of the MPEP recites: Where the claimed and prior art products are substantially identical in composition, or are produced by identical or substantially identical processes, a *prima facie* case of anticipation has been established (See *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433. CCPA 1977). Thus, since the scope of the claims reads upon any cell that is the product of the method disclosed in the prior art, the claimed product is rejected under 35 U.S.C. 102(b).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

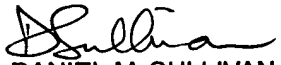
15. Claims 5, 10, 12, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawasaki et al. *Generation of dopaminergic neurons and pigmented epithelia from primate ES cells by stromal cell-derived inducing activity*, Proceedings of the National Academy of Sciences USA 99(3):1580-1585, published on February 5, 2002, as applied to Claims 1-4, 6, 7, 9, 11, 14, 15, 17 and 18 above.

16. Claims 5, 10, 12, and 13 of the instant application recite a method of producing lens cells that is anticipated by Kawasaki reference in each limitation **except** wherein it states, in the differentiation step, plating at a "cell density of 2.5 colonies/cm^2 to 4.0 colonies/cm^2", which the disclosure recites as "equivalent to about 200 to 300 colonies when converted in the number of colonies per culture dish, 10 cm in diameter" (page 9 paragraph 2, lines 3-6). The Kawasaki reference teaches ES cells plated "at a density of 500 clumps/ 10 cm dish", and as stated above, examiner is asserting that it would be immediately apparent to one of ordinary skill in the art of cell culture that the "colonies" of the claim are equivalent to the "clumps" of cells described by the reference. Section 2144.05 (IIA) of the MPEP discusses the obviousness of ranges and states: "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." The disclosure gives no evidence demonstrating a critical importance of **excluding** a colony density of 500 clumps/colonies, as taught by the prior art. Instead, the only data the disclosure provides is that lens cell production increased significantly at concentrations defined as "greater than 200 colonies/dish" (Figures 5 and 6). Thus, claimed process performed by plating cells at a density greater than 200 colonies/clumps per dish, is deemed *prima facie* obvious over the prior art which teaches the identical process performed with "500 clumps/ 10 cm dish".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on Monday-Thursday 6:30AM-4:00 PM & ALT. Fridays, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on (571) 272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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PRIMARY EXAMINER